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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte HANS BAER, THOMAS FUERST,
GERHARD RENNER, and MICHAEL GOTTSCHALK[1]

Appeal 2014-008588
Application 13/256,694
Technology Center 1600

Before ULRIKE W. JENKS, KIMBERLY McGRAW, and
KRISTI L. R. SAWERT, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to an ethanol resistant controlled release pharmaceutical coating. The Examiner rejects the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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[1] According to Appellants, the Real Party in Interest is Evonik Degussa GmbH. (App. Br. 1.)

STATEMENT OF THE CASE

The Specification explains that in order for a pharmaceutical composition to be effective, it is important that the active agent reach therapeutic levels in the blood stream. "A problem exists in that the ideal ratios assumed for the release of active ingredient during the design of a pharmaceutical composition can be altered by the general living habits, thoughtlessness or by addictive behaviour of the patients with respect to the use of ethanol or ethanol-containing drinks." (Spec. 3:9–13.) In order to avoid dosing errors due to lifestyle habits, including alcohol consumption, the Specification teaches adding an ethanol resistance conferring coating to the pharmaceutical composition. The purpose of the coating is "to alleviate or to avoid the possibly fatal consequences of intentional or inadvertent misuse or abuse" when taking the pharmaceutical composition in conjunction with ethanol containing beverages. (Spec. 17:29–30.)

Claims 1–5, 9, 10, 12, 13, 15–23, 25–32, 36, and 37 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. Claim 1 is representative of the claims on appeal, and reads as follows:

> Claim 1: A controlled release pharmaceutical composition, comprising a core comprising a pharmaceutical active ingredient, wherein:
>
> the core is coated with an ethanol resistance conferring coating layer, which confers ethanol resistance to a release profile of the pharmaceutical active ingredient under in-vitro conditions at pH 1.2 and/or at pH 6.8 in a buffered medium;
>
> wherein *ethanol resistance means that the release profile is not accelerated by more than 20 % and is not delayed by more than 20 % under the influence of a 40 % ethanol-containing medium in comparison to a release profile of a medium without ethanol*;
>
> the coating layer comprises at least 70 % by weight of a

mixture of a polymeric portion a) and an excipients portion b);
the polymeric portion a) comprises 60 to 99% by weight of a water insoluble, essentially neutral vinyl polymer or copolymer; and
the excipients portion b) comprises:
b1) 100 to 250 % by weight of a non-porous inert lubricant;
b2) 1 to 35 % by weight of a cellulosic compound;
b3) 0.1 to 25 % by weight of an emulsifier; and additionally or alternatively to b3),
b4) 0.1 to 30 % by weight of a plasticizer,
wherein the percent (%) by weight of each excipient is based on the dry weight of the polymeric portion a).

(App. Br. Claims Appendix I (emphasis added)).

Appellants seek review of the Examiner's rejection of claims 1–5, 9, 10, 12, 13, 15–23, 25–32, 36, and 37 under 35 U.S.C. §103(a) over Mehta[2] and Petereit.[3]

The issue is: Does the preponderance of the evidence of record support the Examiner's conclusion that the combination of references renders the claimed controlled release coating obvious?

Findings of Fact

FF1. Mehta teaches making "[a]n opioid-antagonist oral dosage form which does not release a therapeutically effective amount of the opioid antagonist when the oral dosage form is orally administered to a human being, but whereby a physical alteration of the oral dosage form results in a release of the therapeutically effective amount of the opioid antagonist." (Mehta Abstract). Mehta teaches that if an oral

[2] Mehta et al., US 2004/0202717 A1, published Oct. 14, 2004 ("Mehta").
[3] Petereit et al., US 2005/0079216 A1, published Apr. 14, 2005 ("Petereit").

dosage form containing an opioid and an opioid-antagonist is physically altered (e.g., crushed), the opioid-antagonist is released in amount effective to prevent the abuse of the opioid. (Mehta ¶¶ 1, 9, 10.)

FF2. Mehta teaches the production of an oral dosage form made in a two-step process. "Step 1: applying an opioid antagonist layer to a biologically inert pellet," wherein the layer contains: naltrexone hydrochloride, hydroxypropylmethyl cellulose (HPMC) (methocel E6 10% solution) (i.e., 90% water), purified water, simethicone 30% emulsion (i.e., 70% water), and 25/30 mesh sugar spheres. (Mehta ¶ 48). "Step 2: applying a non-releasing membrane to the coated pellets of Example 1 from step 1 [containing naltrexone (opioid antagonist) potency of 6.2%]" wherein the non release layer contains: Eudragit NE 30D 30% dispersion, and magnesium stearate 15 % suspension spheres. (Mehta ¶ 51.)

FF3. Mehta teaches that "the therapeutically effective amount of the naltrexone is still not released from the dosage form after about 14 to 24 hours, as only 5.7% of the naltrexone has been released from the dosage form after about 24 hours . . . which is [an amount] insufficient to block or neutralize the intended analgesic effect of an opioid agonist." (Mehta ¶ 57.)

FF4. Mehta also teaches that "[t]he opioid-antagonist layer may also include a suitable carrier, diluent, surfactant and/or lubricant." (Mehta ¶ 24; *see also* ¶ 35 ("The opioid-antagonist layer, the opioid-antagonist formulation, and/or the non-releasing membrane of the invention may each further comprise diluents, carriers, fillers and

other pharmaceutical additives which may or may not effect [sic] the rate of release of the opioid antagonist from the oral dosage form of the invention").)

FF5. Petereit teaches "drug form comprising pellets and/or active ingredient matrix, the tablets, pellets and/or active ingredient matrix comprising an active pharmaceutical substance and a copolymer as coating agent and/or binder, and, if desired, a core and pharmaceutically customary excipients." (Petereit ¶ 18.) "In an active ingredient matrix the copolymer acts as a binder for the active ingredient." (Petereit ¶ 56.) Pharmaceutical customary excipients include plasticizers such as for example "triethyl citrate" among others (*see* Petereit ¶ 77) and also encompass "stabilizers, dyes, antioxidants, wetting agents, pigments, gloss agents, etc. (*See* Petereit ¶ 79.)

Principle of Law

Obviousness "requires a suggestion of all limitations in a claim," *CFMT, Inc. v. Yieldup Int'l Corp*., 349 F.3d 1333, 1342 (Fed. Cir. 2003) and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 418 (2007). "Obviousness may not be established using hindsight or in view of the teachings or suggestions of the inventor." *Para-Ordnance Mfg. v. SGS Importers Int'l*, 73 F.3d 1085, 1087 (Fed. Cir. 1995) (citing *W.L. Gore & Assocs., Inc. v. Garlock, Inc.,* 721 F.2d 1540, 1551, 1553 (Fed. Cir. 1983)). "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the

modification." *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992).

Analysis

Mehta teaches the production of oral dosage forms that are resistant to physical alteration (FF1) and that do not release a significant amount of their content during normal use (FF3). Mehta exemplifies the production of the oral dosage form by first coating the active ingredient and HPMC mixture onto an inert pellet that then provides a further coating with a non-releasing membrane (FF2). Mehta also teaches that the active ingredient layer and the separate non-releasing layer can include additional substances such as diluents, carrier, fillers and other additives (FF4).

According to the Examiner, "Mehta teaches the major structure in a substantially similar manner as the claimed invention except that Mehta do[es] not explicitly teach polyoxyethylene(20)-sorbitan-monooleate as emulsifier and in the alternative trietyl citrate as a plasticizer being added together with the Eudragit NE 30D." (Ans. 15). The Examiner states that although "Mehta does not specifically teach the amount of excipients as recited in claim 1 . . . [t]hese deficiencies are cured by the teachings of Petereit" (*id.* at 7).

Petereit teaches the production of pharmaceutical dosage forms that can include a mixture of active ingredient and copolymer in conjunction with other customary pharmaceutical ingredients (FF5).

Based on the combination of references, the Examiner concludes that "[o]ne of ordinary skill in the art would have been motivated to incorporate the excipients [as taught by Petereit] in such an amount because they are conventional ingredients that are controllable by one of ordinary skill in the

art as demonstrated by Petereit." (Ans. 10). Furthermore, because "the amount of the coating relative to the core is also a results-effective variable, the determination of the optimum amount of coating would also be routine experimentation" (*id.* at 11). "An ordinary skilled artisan would have had a reasonable chance of success in combining the teachings of Mehta and Petereit et al. because both references teach similar dosage forms comprising a controlled release controlling layer made from substantially similar or same polymers" (*id.*).

Appellants contend that "[t]here is no issue herein whether the presently-recited excipients have been used before in, for example, controlled release pharmaceutical compositions. They have. Rather, it is the particular combination and the respective amounts of these components, and the unique ethanol resistance effect of the combination, that distinguish the prior art." (Reply Br. 3).

Based on the record before us, we agree with Appellants' position that the Examiner has not established by a preponderance of the evidence that the claimed invention would have been obvious over the asserted prior art references. Although we recognize that the Examiner has directed us to disclosures in the references that show the use of the claimed individual components[4] (see FF1–FF5), what is missing from the Examiner's analysis,

[4] The Examiner notes that there was a species election made during prosecution and "the rejections on the merits [are] based on this species election." (Ans. 12.) Specifically, "Naloxone as the pharmaceutical active ingredient, Eudragit® NE as the water insoluble essentially neutral vinyl polymer or copolymer, talc as the non-porous inert lubricant, HPMC as the cellulose compound, polyoxyethylene(20)-sorbitan-monooleate as emulsifier, triethylcitrate as plasticizer." (Ans. 12.)

however, is evidence that an artisan would have a reason to modify the combination of components so that "the release profile is not accelerated by more than 20 % and is not delayed by more than 20 % under the influence of a 40 % ethanol-containing medium in comparison to a release profile of a medium without ethanol" as claimed. *See KSR*, 550 U.S. at 418 (obviousness rejections require "some articulated reasoning with some rational underpinning"). In other words, although we agree with the Examiner's position that one of ordinary skill in the art can manipulate the individual components as disclosed in Mehta and Petereit and obtain numerous different release profiles, the Examiner has not articulated a reason why one of ordinary skill in the art would have made such a modification to arrive at the composition as claimed.

Notably, Mehta is directed to pharmaceutical compositions having a non-releasing membrane where the membrane does not release the active ingredient unless the dosage form is physically altered (e.g., crushed). In contrast, Petereit is directed to oral dosage forms wherein, based on coat thickness, the release profile can be manipulated to rapidly release the active or to delay the release of active until deep into the intestine. (Petereit ¶¶ 108–113.) There is nothing in the references, nor in the Examiner's stated rationale, that explains a need to manipulate pharmaceutical formulations so that they are not affected by the presence of ethanol.

We are also not persuaded by the Examiner's overlapping range and/or results effective variable argument because this too requires some knowledge of an end result, i.e. in this case the claimed ethanol release profile. Again, although we recognize that Mehta and Petereit disclose the individual components, we note that none of the examples in the references

contain polymeric portion a) and excipients portion b) as claimed. Without having an articulated reason to adjust the formulations to achieve a particular result, one ordinary skill would not necessarily arrive at the claimed composition.

Based on the evidence of the entire record, we do not sustain the Examiner's rejection. In summary, the Examiner has not provided evidence sufficient to support a conclusion that a person of ordinary skill in the art would have considered it obvious to combine the disclosed elements in the manner claimed. We therefore reverse the rejection of claim 1, as well as dependent claims 2–5, 9, 10, 12, 13, 15–23, 25–32, 36, and 37.

SUMMARY

We reverse the rejection of claims 1–5, 9, 10, 12, 13, 15–23, 25–32, 36 and 37.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

REVERSED